

**THE SIGNIFICANCE OF SERUM C-
REACTIVE PROTEIN ESTIMATION IN
ACUTE MENINGITIS IN ADULTS**

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CERTIFICATE

This is to certify that the dissertation titled “**THE SIGNIFICANCE OF SERUM C-REACTIVE PROTEIN ESTIMATION IN ACUTE MENINGITIS IN ADULTS**” is the Bonafide original work of **Dr. K. GOWRI SHANKAR** in partial fulfillment of the requirement for M.D. Branch –I (General Medicine) examination of the Tamil Nadu Dr. M. G. R. Medical University to be held in March 2007. The period of study is from August 2005 to September 2006.

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DECLARATION

I **Dr. K. GOWRI SHANKAR**, solemnly declare that the dissertation titled, “**THE SIGNIFICANCE OF SERUM C-REACTIVE PROTEIN ESTIMATION IN ACUTE MENINGITIS IN ADULTS**” was done by me at Govt. Stanley Medical College and Hospital during 2005– 2006 under the guidance and supervision of my unit chief **Prof. Dr. K. RAJENDRAN, M.D.,**

The dissertation is submitted to Tamil Nadu Dr. M.G.R Medical University towards the partial fulfillment of requirement for the award of M.D Degree (Branch – I) in General Medicine.

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INTRODUCTION

The evolution of clinical signs and symptoms produced by meningitis or encephalitis varies greatly. Few conditions in medicine require as rapid and accurate therapeutic intervention as acute pyogenic meningitis and viral meningitis, yet meningitis can also occur in chronic and recurrent forms. The major problem presented by patients with meningitis is rapid determination of its aetiology, the specific basis on which selection of potentially effective antimicrobial therapy is predicted. Thus, the clinician must sort out the form of clinical presentation, assess the rapidity of its evolution, and make a specific aetiological diagnosis.

The examination of cerebrospinal fluid is an essential and often critical tool in the evaluation and management of patients with meningitis. If interpreted carefully, the cerebrospinal fluid (CSF) analysis, can be very helpful in guiding the diagnostic evaluation and management of patients.

Although examination of a Gram's stain of spinal fluid often defines the causative agent, this is not always the case. Cultures have the drawback of the time required, 24 to 48 hours or more to become positive, an unacceptable delay in initiating the treatment.

Deivanayagam. N et al (1993)²¹ Clinical Epidemiology Unit, Madras Medical College, have declared that in developing countries, differentiating bacterial meningitis from viral meningitis and tuberculous meningitis is not easy.

Not all medical centers have viral diagnostic laboratories at their disposal. Moreover, serological confirmation of a viral infection is usually of academic interest, since by the time its result is available, the patients would have recovered or otherwise, it never determines specific therapy.

Further, the cost of antiviral therapy is very high when compared to antimicrobial therapy. So, in developing countries like India, we can not institute empirical antiviral therapy to all patients of suspected viral meningitis. Therefore, several different techniques to discriminate rapidly between viral meningitis and bacterial meningitis have been evaluated. These include Counter Immuno Electrophoresis (CIE) of the CSF for the immunoglobulins, lactic acid, creatine phosphokinase isoenzyme and C-reactive protein. **Brown et al (1978)¹⁵**.

Because of easy availability of the kit and simplicity of the procedure, serum C-reactive protein (CRP) was selected to differentiate viral meningitis and bacterial meningitis, which is elevated in the latter, were observed in the selection of cases.

Further, CRP was used only to differentiate bacterial meningitis from other meningitis, but not for the diagnosis of meningitis which was done only by routine clinical methods.

AIM

To evaluate the efficacy of serum C-Reactive Protein in differentiating bacterial meningitis from viral meningitis.

REVIEW OF LITERATURE

C-reactive Protein:

Name Origin:

During studies of the pneumococcal immune response **Tillett & Francis (1930)**¹⁰³ found that before the critical fever crisis, the patient's sera contained a component that precipitated a common factor in crude extracts of all pneumococci; fraction C. (**Gupta and et al. 1987**)³⁹.

Chemistry:

CRP is a protein composed of five identical non-covalently bound, globular subunits of molecular weight 21,000. This pentraxin molecule preferentially adopts a planar orientation and may stack in two layers to form decamers. The single peptide chain contains 187 amino acids with only two halfcystine residues stabilizing the conformation by forming a disulfide bond (**Oliveria et al, 1979**)⁷⁰.

The primary structure shows no repeating sequences and very few homologies with other proteins except with serum amyloid plasma P-component. CRP migrates as a beta globulin on agarose gel electrophoresis in the absence of Ca^{2+} and as a slow gamma globulin in the presence of Ca^{2+} or Ba^{2+} . Each CRP subunit can bind one Ca^{2+} which explains its effect on the electrophoretic mobility. Calcium ion induces a conformational change in each subunit and strongly

increases affinity of CRP for a series of organic phosphates and for sulphated polysaccharides. Phosphorylcholine has been identified as the binding constituent of the pneumococcal C- polysaccharide which caused the phenomenon that gave rise to its detection (C-Polysaccharides precipitation and swelling of pneumococcal membranes). (**Sirijai Chingkul S, et al 2005**)⁹³. The Ca²⁺-dependent affinity of CRP for phosphorylcholine, phosphorylated, sulphated or Carboxymethylated polysaccharides has been utilized as an efficient chromatographic step in the purification of CRP from a wide variety of animal species (crabs, fishes, birds and mammals) (**Baltz et al, 1981**)⁷.

Physiology:

CRP is an extra cellular protein, synthesized mainly in the hepatocytes. A sub-population of the large lymphocytes, the natural killer cells – are said to have endogenous CRP on their surface membranes. The secretion rate is low in healthy subjects and no hepatic store exists. The Plasma concentration is below 5 mg/L and may vary to as low as 50 µ/L (**Kindmark, 1972**)⁵⁶. Though CRP turnover has not been measured at the normal steady state, the synthetic rate is estimated to be in the order of 1-10mg per day (**MacIntyre et al, 1982**)⁶³. CRP is considered to constitute a link in one mechanism for eliminating necrotic cells and foreign particles in the body (**Kushner & Kaplan, 1961**)⁵⁸. This protective system was an earlier evolutionary development than the Ig system. CRP analogues occur normally in the extra cellular fluids of lower animals in concentrations 100 times

as high as those in mammals, which only begin to reach similar high values during very intense inflammatory reaction. **(Vaishnavi c et al 1992)¹⁰⁷**.

Discussion of the molecular basis of effects of the CRP has been focused on its Ca^{2+} mediated linkage to phosphorylcholine and acid polysaccharides. The disordered architecture of the phospholipid bilayer of cell membranes opens the way for calcium ion-mediated linkage of CRP, which then adopts a conformation with affinity of C1q of the C1 complex. This linkage triggers activation of the complement cascade along the classical pathway, and reactions characteristics of an acute inflammatory response follow. **(Bengershom E. etal 1995)¹⁰**. The unique binding of CRP to the C-polysaccharide of pneumococcal membranes induces in vivo, an enhanced phagocytosis of the microorganisms. Pneumococci are efficiently cleared by the spleen after linkage of CRP Clinically it has been recognized that severe pneumococcal infections are frequent in splenectomised patients **(Gopal & Bisno, 1977)³⁷**.

Pathophysiology:

The CRP linkage to selective polysaccharides of some bacterial membranes apparently contributes to induce protective reactions in the host organism even when no specific antibodies are present **(Volanakis, 1982)¹⁰⁹**. The recognized in vivo effects of CRP complexes concern activation of the classical pathway of complement and activation of phagocytes. These effects represent an early induc

tion of host reactions that are similarly, but probably more efficiently, triggered by specific antibodies when they are present. **(Bengershom et al 1995)¹⁰** Cell death anywhere in the body induces local cellular and vascular reaction and changes in the composition of the extra cellular fluids embraced by the concept inflammatory response. This includes an altered protein synthesis in hepatocytes and in the phagocytic cells which accumulate around the injured cells. Messengers carried to the liver induce a metabolic shift in the hepatocytes. This is characterized by a decreased synthesis of transport proteins and an increased synthesis of protective proteins-particularly Acute Phase (AP) proteins **(Kushner, 1982)⁵⁹**. (Fig.1) AP protein inactivate strongly reactive molecules such as proteolytic enzymes and oxygen derived free radicals, released or secreted from accumulating phagocytic cells or from injured cells. The continuous exchange of protective proteins, between plasma and the intracellular fluids, serve as a buffer system that counteracts the rapid intercellular which effect the mobility of the tissue fixed macrophages. Interleukin 1 is a biologically very potent (12,000-15,000 dalton) polypeptide which is active in the 10^{-10} to 10^{-15} concentration range. The hepatic CRP synthesis is rapidly triggered by interleukin 1 and the plasma concentration of CRP starts to rise after about 6 hours. Experimental data **(Mac Intyre et al, 1982)⁶³** support the idea that a key function of the reticuloendothelial macrophage system is to induce accelerated hepatic CRP biosynthesis as much as 100 times (1g/d) within the first few days following severe tissue lesion. As the inducer disappears CRP synthesis declines to its normal very low rate after a delay, the

length of which is primarily determined by the decay of its hepatic mRNA ($t_{1/2} = 4\text{h}$). (Ballou et al 1992)⁹.

The molecular size of CRP suggests an equal distribution between plasma and intercellular fluids at a steady state. The $t_{1/2}$ of CRP in human plasma is of the order of 1-2 days, which is shorter than those of all other plasma proteins. The concentration of CRP reflects the local activity of an inflammation better than other acute phase proteins because both its faster rise following acute tissue lesion and its decline on remission is faster than that of other plasma proteins. (Paradowski et al 1998)⁷².

Clinical and biochemical advantages

CRP is the fastest reacting and most sensitive indicator of an acute inflammatory reaction. It is an useful aid in preliminary differentiation between acute bacterial and viral infections with sensitivity and specificity rates of 100% and 98% respectively. (Azeem Shelkh et al 2001)⁶.

The increase in plasma concentration of CRP, varying from several fold increases with slight tissue lesion to hundred folds with severe lesion, renders the CRP concentration a very good semi quantitative indicator of the inflammatory process. Since the survival time of CRP in the circulation is shorter than that of other acute phase reactants remission is quickly reflected in a falling CRP concentration. (Paradowski et al 1998)⁷². The fall in CRP is a sensitive indicator

of recovery from infection and provide the earliest check to therapeutic response. The slide agglutination tests of anti CRP covered particles is the simple qualitative and quantitative test, sufficiently specific and most sensitive. **(Diculencu et al 1995)²⁴**.

The serum CRP (S-CRP) can be used to differentiate pyogenic meningitis or acute meningitis due to other causes. S-CRP of more than 48 mg/L is sensitive and specific for bacterial infection. A fall in the S-CRP concentration is a sensitive indicator of recovery from infection and provides an earliest clue to the therapeutic response, long before a fall in temperature. **(Stearman M, et al 1994)⁹⁷**.

MATERIALS AND METHODS

Fifty cases with definite clinical signs and symptoms of acute meningitis admitted in **Govt. Stanley Hospital, Chennai** during the period **August 2005 to September 2006** were taken up for the study.

All the cases have shown the clinical signs and symptoms of meningeal infection. The following clinical signs and symptoms were given at most importance for the selection of cases.

1. Fever of acute onset
2. Neck Stiffness : Passive flexion of the neck is difficult or Impossible
3. Kernig's sign : With the patient on supine posture, when the hip is fully flexed the passive extension of the patient's knee, causes pain and spasm of the hamstrings in meningeal irritation affecting the lower part of the spinal subarachnoid space.
4. Brudzinski's Sign : (i) Contralateral reflex or Sign:
On passive flexion of the leg on one side, a similar movement occurs in the opposite leg.

(ii) Neck Sign : When the neck is passively flexed, flexion of the hip and knee occur.

5. Symptoms of increased intracranial pressure like Headache, Vomiting.

6. Altered Sensorium :

All the selected cases were investigated for serum C-reactive protein levels which was done by Rapid latex test. CSF study was done in all cases, to confirm the S-CRP findings. In one case lumbar puncture was not done because of bilateral papilledema.

CSF Analysis :

The cerebrospinal fluid was tested for

- a. Colour : Clear, turbid, Opalescent, High coloured and/or blood stained.
- b. Tension : Normal or elevated
- c. Cell count : Cerebrospinal fluid was stained for cell count and examined under High power field for rapid results.
- d. Staining : A drop of centrifuged CSF was placed over the glass slide, dried and stained for AFB and Gram's stain.

- e. Cob web : 2ml of CSF was collected in a test tube and mounted in a rack. Examined after 24 hours for the presence of cobweb. If present, the precipitate was again centrifuged and stained for AFB.
- f. Culture : CSF was sent for culture and sensitivity.
- g. Biochemical Analysis : CSF was sent for estimation of globulin, proteins, sugar and chloride.

The results were correlated with the results of S-CRP levels and the cases were differentiated into bacterial meningitis or meningitis due to other causes.

Inclusion Criteria

1. Above 12 years of age
2. History suggestive of meningitis
3. Neck Rigidity

Criteria Observed for serum CRP testing

All cases which had the following history were excluded from the study in order to avoid false positive S-CRP results.

1. Recent injury of any kind.
2. Recent surgery.

3. Patients in the immediate post-partum period,
4. Known case of Rheumatic Heart Disease (according to modified Jones Criteria)
5. Known case of Rheumatoid arthritis (according to ARA diagnostic Criteria)
6. Known case of acute or chronic glomerular nephritis and all cases of Genito- Urinary tract infection.
7. Focal infections like pneumonic consolidation, infections of skin etc.,

PRINCIPLE

Principle is based on a rapid agglutination procedure for the direct detection and semi-quantitation (on slide) of C-reactive protein (CRP). The reagent, a latex particle suspension coated with specific anti-human C-reactive protein antibodies, agglutinates in the presence of CRP in patient serum.

REAGENTS

- | | | |
|----|---|-------------------------|
| a. | CRP LATEX:
Suspension of polystyrene particles coated with anti-human CRP goat antibodies. | 1 x 1.5 ml / 1 x 2.5 ml |
| b. | CRP POSITIVE CONTROL
Human pooled serum | 1 x 0.5 ml |
| c. | CRP NEGATIVE CONTROL
Human pooled serum | 1 x 0.5 ml |

- d. GLYCINE SALINE BUFFER CONCENTRATE 1 x 5 ml
Dilute 1.10 with distilled water.
- e. Accessories
- | | For 30 T | For 50 T |
|--------------------|----------|----------|
| Reaction slide | 1 | 1 |
| Plastic Droppers | 30 | 50 |
| Applicators sticks | 30 | 50 |
| Rubber Teat (Blue) | 1 | 1 |

PRECAUTION

The reagents of human origin, used in the study have been tested and found to be negative for the presence of antibody to HIV I and II as well as for HBs Ag and HCV antibody.

The reagent and controls contain less than 0.1 % of sodium azide.

STORAGE AND STABILITY

1. Stored at 2-8⁰C
2. Protected from light
3. Stability as per kit used.

PREPARATION OF GLYCINE SALINE BUFFER

Glycine saline buffer was prepared by adding 45ml of distilled water to 0.5ml of concentrate glycine saline buffer.

SENSITIVITY

The CRP sensitivity has been adjusted to detect a minimum of 0.6 mg/dL in the undiluted sample.

SAMPLE

Fresh serum sample (free of haemolysis).

QUALITATIVE TEST

All reagents, as well as the sample were allowed to reach room temperature, and mixed well, before use.

1. One drop of serum sample was placed on to the slide with the help of disposable serum dropper.
2. One drop of CRP-Latex antigen was added to the above drop and mixed well with disposable applicator stick.
3. Slide was gently rocked to and fro for 2 minutes and examined under a good light source for agglutination within 2 minutes.
4. For positive & negative controls, the same procedure as mentioned above, was followed, by taking control serum from respective vials.

RESULT AND INTERPRETATION

POSITIVE RESULTS

The presence of agglutination indicates concentration of CRP in the sample equal to or greater than 0.6 mg/dL.

NEGATIVE RESULTS

The lack of agglutination indicates a CRP concentration lower than 0.6 mg/dL. in the sample.

SEMI-QUANTITATIVE TEST-BY SERIAL DILUTION METHODOLOGY

1. 50µL dilute Glycine saline Buffer was placed on to each of five circles of the slide.
2. Using a 50µL (0.05 mL) micropipette, 50µl (0.05ml) of the serum sample was added to the drop of Glycine – Saline Buffer in 1st circle.
3. Using the sample micro – pipette, the sample was mixed with saline by aspirating back and forth several times. 50µl (0.05ml) from 1st circle was aspirated and transferred to 2nd circle. The same operation was repeated upto the 5th circle. 0.05ml from 5th circle was aspired and discarded.

Following dilutions were obtained

Dilution : 1/2 1/4 1/8 1/16 1/32

4. One drop of CRP-latex Antigen was added, to each of the above circles and the slide was rocked gently to and fro for 2 minutes. Agglutination was observed under a good light source.

CALCULATIONS

Whenever S-CRP is negative or positive in 1:2 or 1:4 serum it is taken as <5mg/L and 6mg /L respectively. If positive, in 1:8 dilution, it is 12-18 mg/L and in 1:6 dilution as 24 – 48 mg/L. The reading is taken as >48 mg/l whenever it is positive in 1:32 dilution.

Sl.NO.	Dilution	Qualitative	Quantitative
1.	1/2	(-)	< 5mg/l.
2.	1/4	(+)	6-12 mg/l
3.	1/8	(++)	12-24 mg/l
4.	1/16	(+++)	24-48 mg/l
5.	1/32	(++++)	>48 mg/l

The value of S-CRP in differentiating bacterial from non-bacterial meningitis was cross checked with CSF studies (Sugar, Protein, AFB, gram stain) and serum & CSF cultures.

CSF analysis observed for bacterial meningitis was

CSF Proteins	>	45 mg /dl
CSF Sugars	<	40 mg /dl
CSF Cell count		Raised with predominant polymorphonuclear (PMN) cells

(Harrison 16th edn)

OBSERVATION AND RESULTS

In the study of fifty cases of acute meningitis admitted in Govt. Stanley Hospital, Chennai, the following observations were made in sex incidence, age, clinical presentations, CSF analysis, serum C-reactive protein level and prognosis of the illness as follows:

Sex Incidence:

Fifty cases of acute meningitis infection have been observed. The study showed a male predominance of 56% while the female was 44%. (Table –I)

Table – I

SEX INCIDENCE IN THE STUDY

Sl. No	Sex	Number of patients	Percentage %
1.	Male	28	56%
2.	Female	22	44%

Age Incidence:

It is observed in the study that, 16 cases belong to the age group of 13-20 years (32%), another 14 cases (28%) in 21-40 years group, 16 cases (32%) were from 41-60 years group and 4 cases (8%) were above 60 years of age. (Table – II)

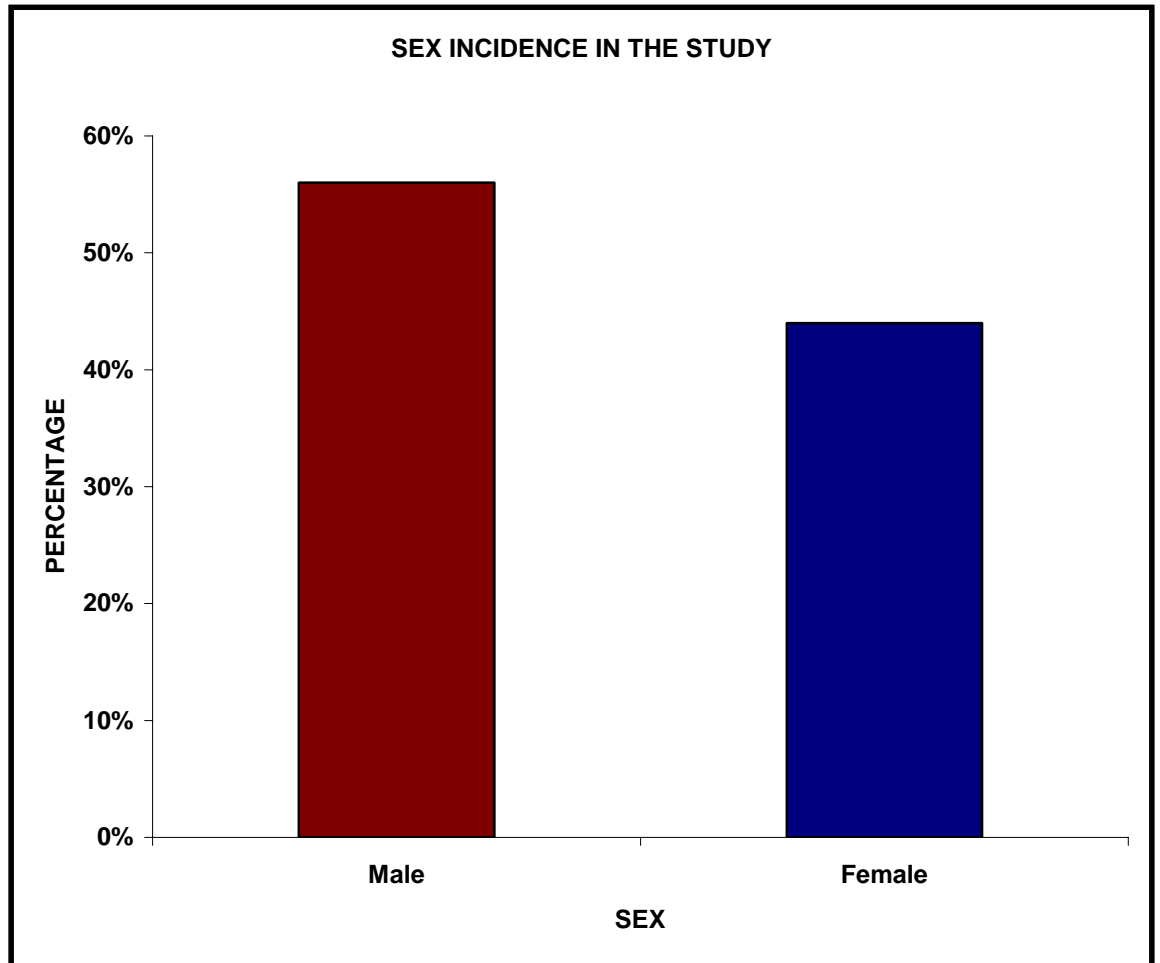


TABLE – II
AGE INCIDENCE IN THE STUDY

Sl. No	Age in Years	Number of patients	Percentage %
1.	13-20	16	32%
2.	21-40	14	28%
3.	41-60	16	32%
4.	>60	4	8%

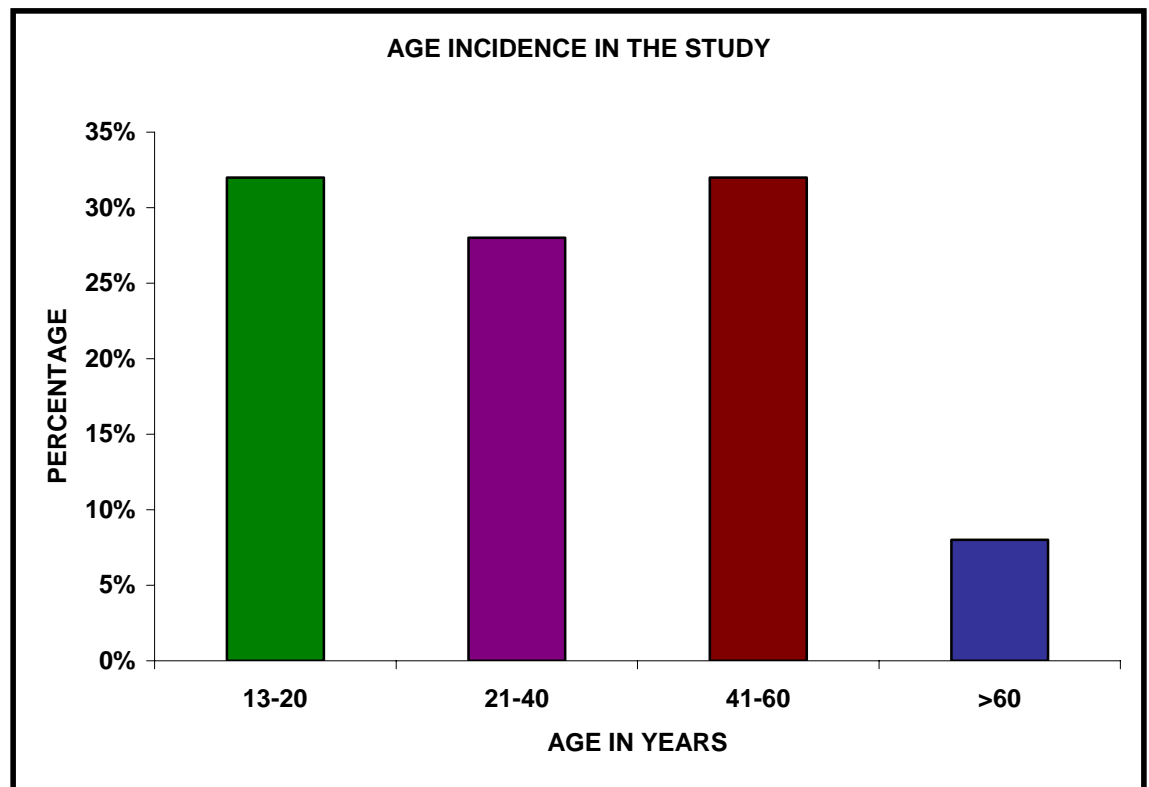
Symptoms:

The sequence of symptoms observed from the study were as follows. 98% (49) of cases presented with fever while 48% (24) presented with vomiting. (Table- III).

TABLE – III
SYMPTOMS TABLE

Sl. No	Symptoms & Sign	Number of patients	Percentage %
1.	Fever	49	98%
2.	Altered Sensorium	41	82%
3.	Head ache	30	60%
4.	Vomiting	24	48%
5.	Neck rigidity	50	100%
6.	Seizures	21	42%
7.	Neurological deficits	20	40%
8.	Abdominal pain & Diarrhoea	5	10%

The incidence of seizure were observed in 42% (21) of cases, 40% (20) had neurological deficits and 10% (5) had abdominal pain and diarrhoea.



Meningeal Signs:

Neck stiffness was seen in all the fifty cases, as it was considered as the prime sign for the selection of cases. Thirty eight cases (76%) were found to have positive Kernig's sign whereas Brudzinski's sign was positive in thirty cases (60%).

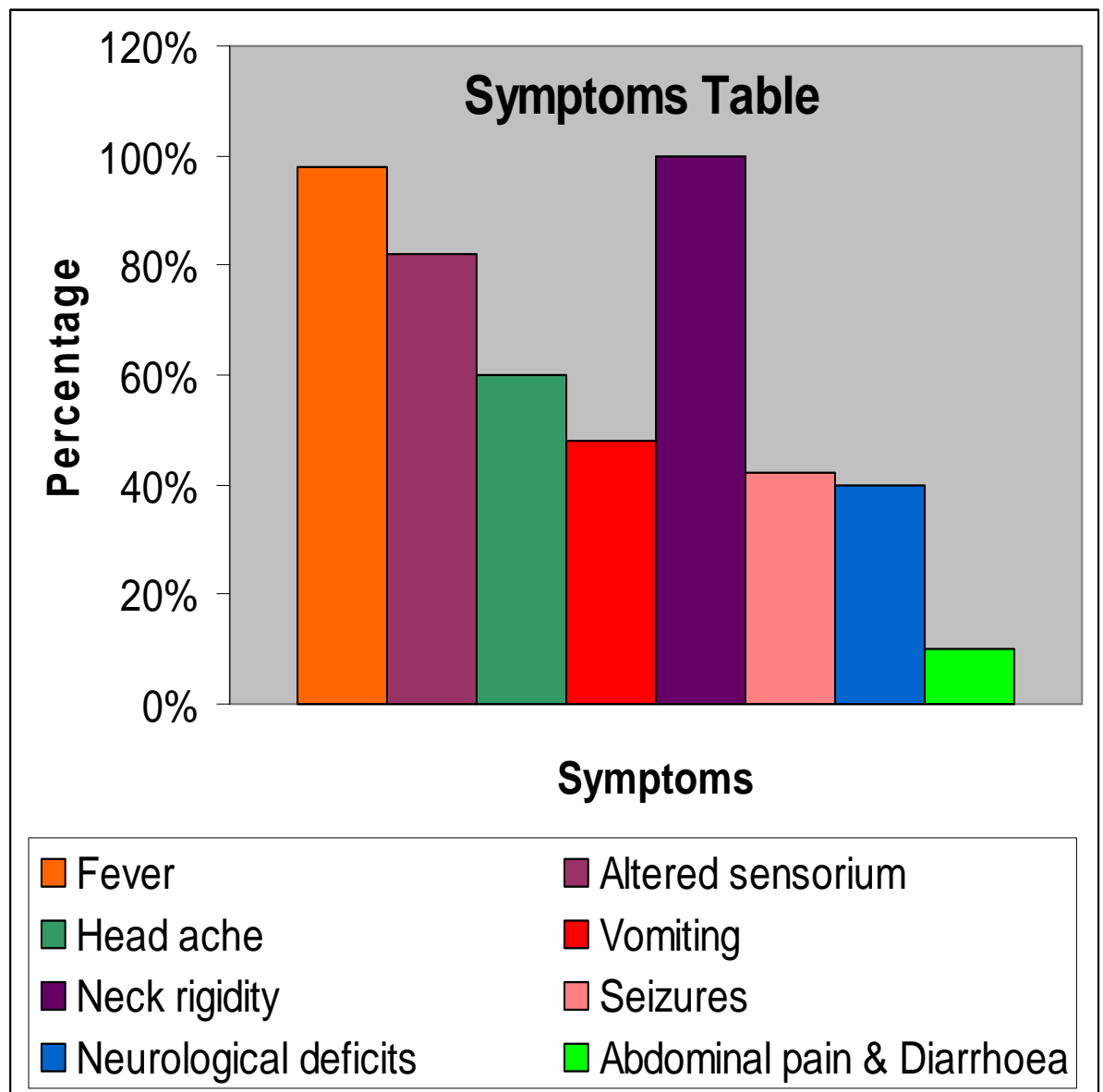
Papilledema

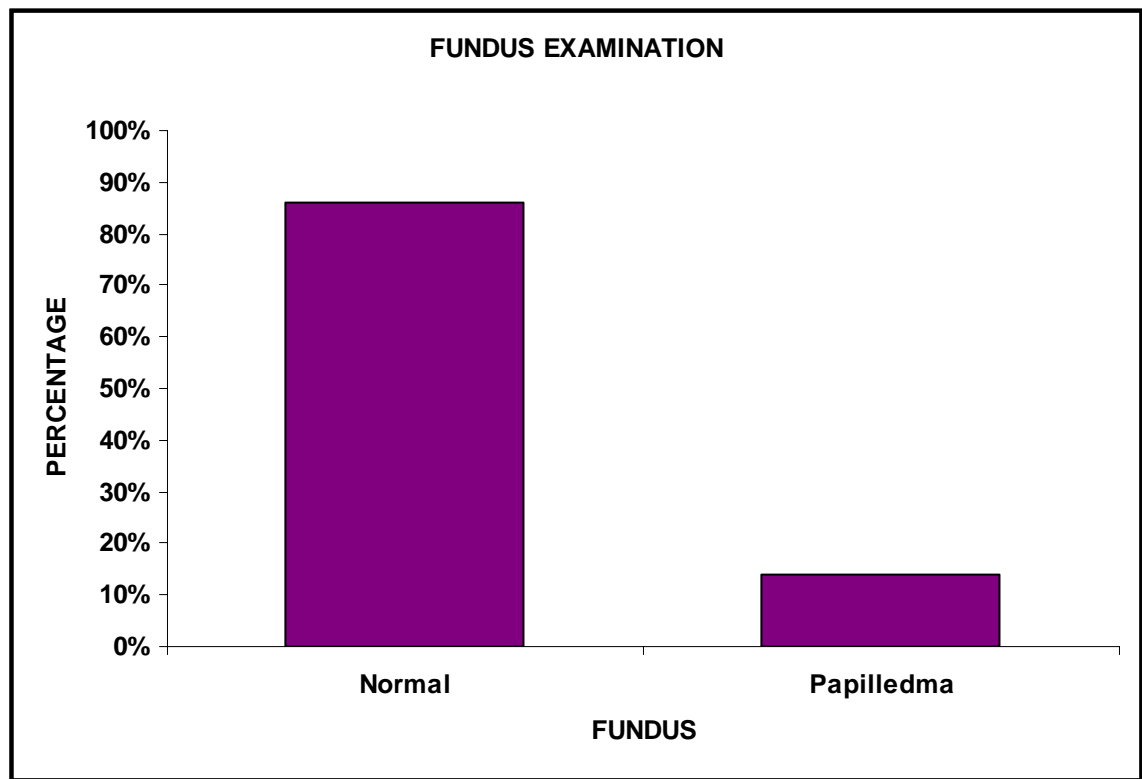
Papilledema was present in seven out of fifty cases. Among them five belong to bacterial meningitis group, of which three expired. The other two who belong to non bacterial group have recovered and are alive.

TABLE – IV

FUNDUS EXAMINATION

Sl. No	Fundus	Number of patients	Percentage %
1.	Normal	43	86%
2.	Papilledema	7	14%





Neurological Deficit:

Abducent Nerve Palsy:

Of the fifty cases, five cases developed VI cranial nerve palsy. Among the five, the VI Cranial nerve palsy was unilateral in four and bilateral in one who has papilledema also.

Three cases belonged to the bacterial meningitis group, of which two were having papilledema. One case belonged to the viral meningitis group, and one belonged to tuberculous meningitis group. Of the five, two expired (Table – V).

TABLE – V
NEUROLOGICAL DEFICITS

Sl. No	Neurological Deficits	Number of patients	Percentage %
1.	Abducent nerve palsy	5 (3B, 1V, 1TB)	10 %
2.	Facial Nerve palsy	4 (1B, 3V)	8 %
3.	Other Cranial Nerve palsy	0	0
4.	Aphasia	4 (1B, 2V, 1TB)	8 %
5.	Hemiparesis	6 (1B, 5V)	12 %
6.	Quadriparesis	1 (V)	2 %

B – Bacterial, V-Viral, TB – Tubercular.

Facial Nerve Palsy

Four cases were found to have unilateral VII cranial nerve palsy of which three belonged to the viral meningitis group, two of them presented with papilledema, hemiparesis and aphasia. All of them survived. (Table – V).

Hemiparesis

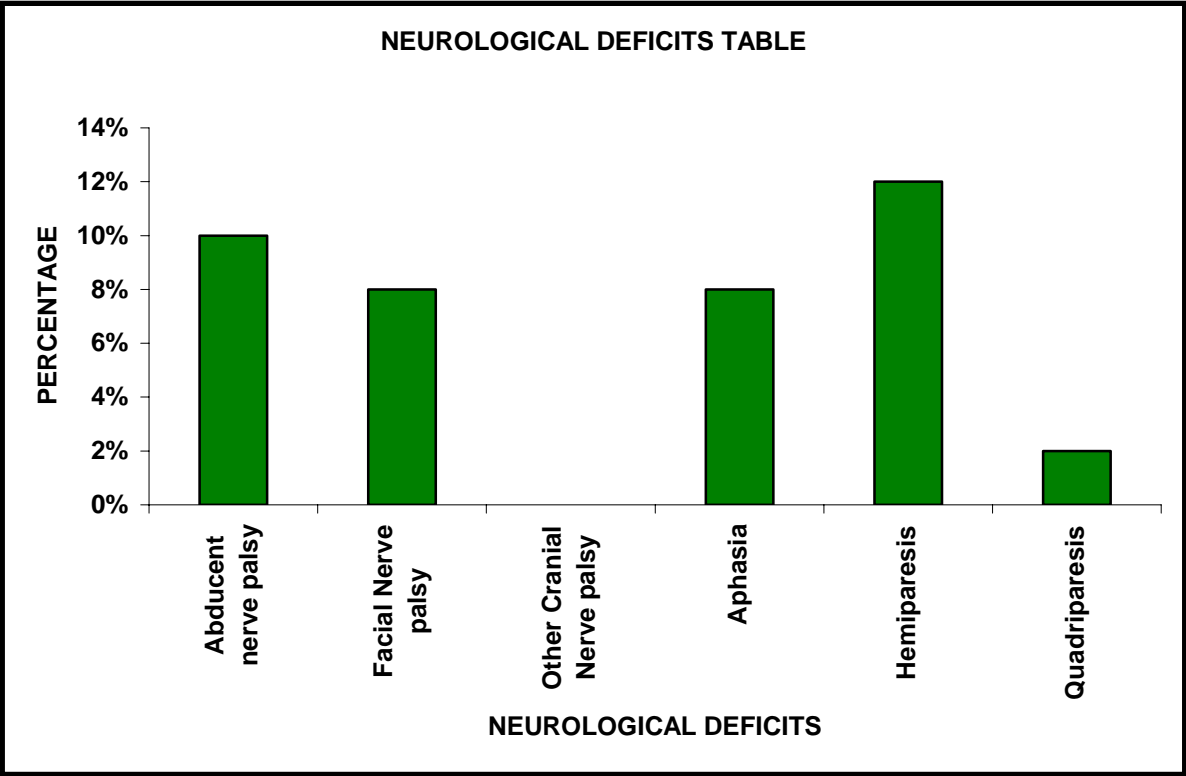
Hemiparesis was observed in six cases. (Table - V). One belonged to the bacterial meningitis group, who had papilledema and VI cranial palsy expired. Five cases belonged to the viral meningitis group. Two had associated papilledema, VII cranial nerve palsy and aphasia.

Aphasia

Four cases developed aphasia during the course of illness. Two had associated papilledema, VII cranial nerve palsy and hemiparesis. Of these, one was bacterial, one tubercular and two of viral origin. (Table V).

Quadripareisis

One case belonged to the viral meningitis group, developed spasticity in all the four limbs, (Table – V) soon became unconscious and expired. No other neurological abnormalities were observed.

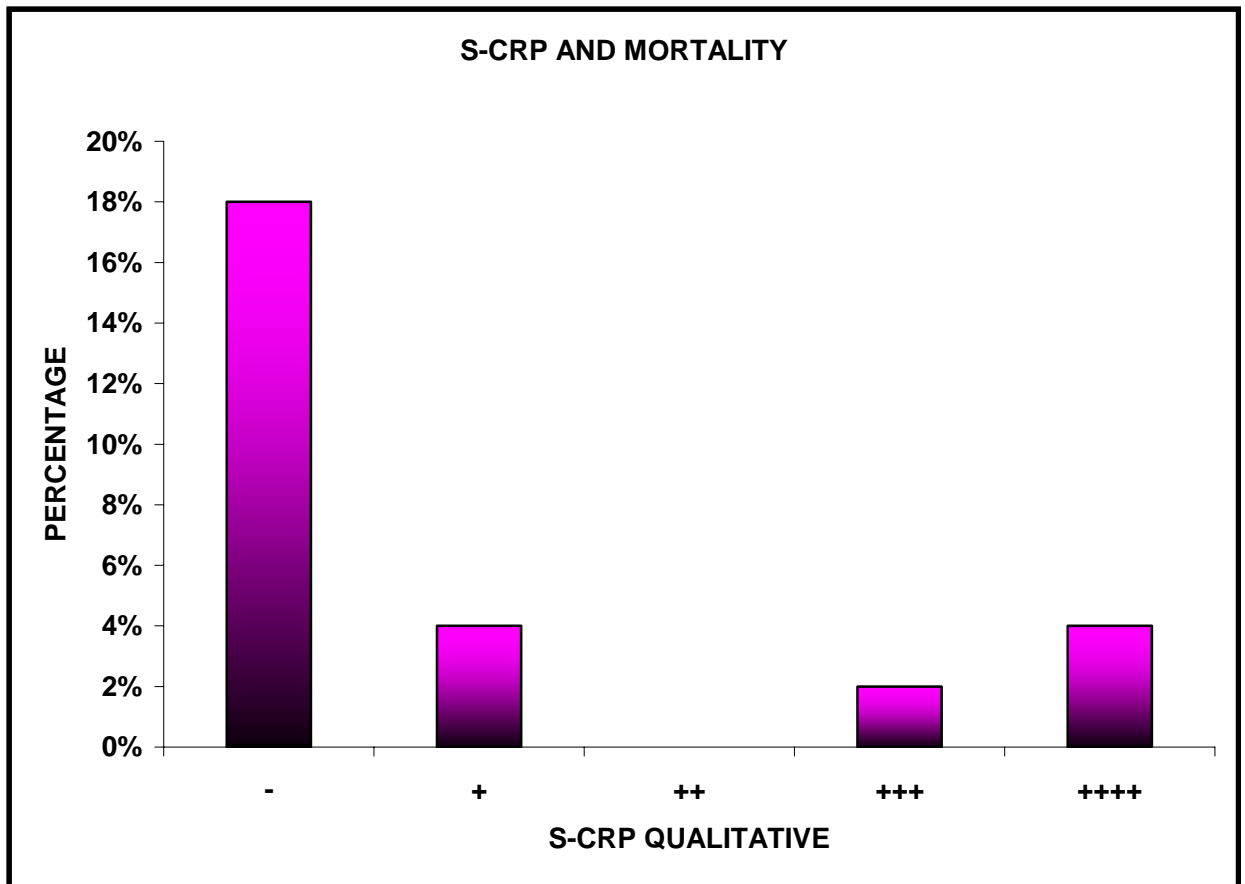


S-CRP and mortality

S-CRP levels were analyzed in all the fifty cases. Sixteen cases (32%) showed negative results for S-CRP indicating a possibility of viral infection. Of these nine cases (18%) expired. Nine cases (18%) were having S-CRP of 6 mg/L level, of which 2 cases (4%) expired. Eight cases (16%) had S-CRP levels 12-18 mg/L level of which there was no mortality. Nine cases (18%) had S-CRP levels 24-48 mg/L, of which one died (2%) and eight cases (16%) were having strongly positive levels of > 48 mgms / L indicating a definite bacterial infection, of which two cases (4%) expired. (Table – V).

TABLE – VI
SERUM – CRP AND MORTALITY

Sl. No	S-CRP (mg/l)	S-CRP Qualitative	Number of patients	Death	Percentage %
1.	<6	-	16	9	18%
2.	6 – 12	+	9	2	4%
3.	12 – 24	++	8	0	0%
4.	24 – 48	+++	9	1	2%
5.	>48	++++	8	2	4%



In 25 cases, S-CRP levels were less than 12 mg/l. of these, 16 cases had SCRP <6 mg/l and 9 cases had SCRP 6-12 mg/l. All these 25 cases were having clinical signs in favour of meningitis or meningoencephalitis and CSF formula in favour of viral infection. The CSF glucose level in all the 25 cases were near normal limit and protein is normal or slightly elevated, indicating the possibility of viral infection.

S-CRP and prognosis

In all fifty cases, S-CRP was done first, at admission, second after three days of hospitalization and the third one before discharge, so as to assess the prognosis of the patient.

Of these, sixteen had shown a rapid fall in S-CRP levels and a very good prognosis. The S-CRP indicated good prognosis earlier than other investigations. One case was having sustained high S-CRP levels and expired despite treatment.

In another eight cases who were positive for S-CRP levels subsequent tests revealed negativity and this again indicated a good prognosis.

In the remaining twenty five cases, the S-CRP levels were negative, subsequently tested again to rule out false negativity but it revealed the same results.

Level of Consciousness and Mortality

It is observed from the study that 4 cases were unconscious at the time of admission. Of them, two between 21-40 years, had history of unconsciousness for 6 hrs. One of them had a S-CRP level of >48 mg/L and the CSF picture in favour of bacterial infection, showed a very good improvement from treatment with antibiotics.

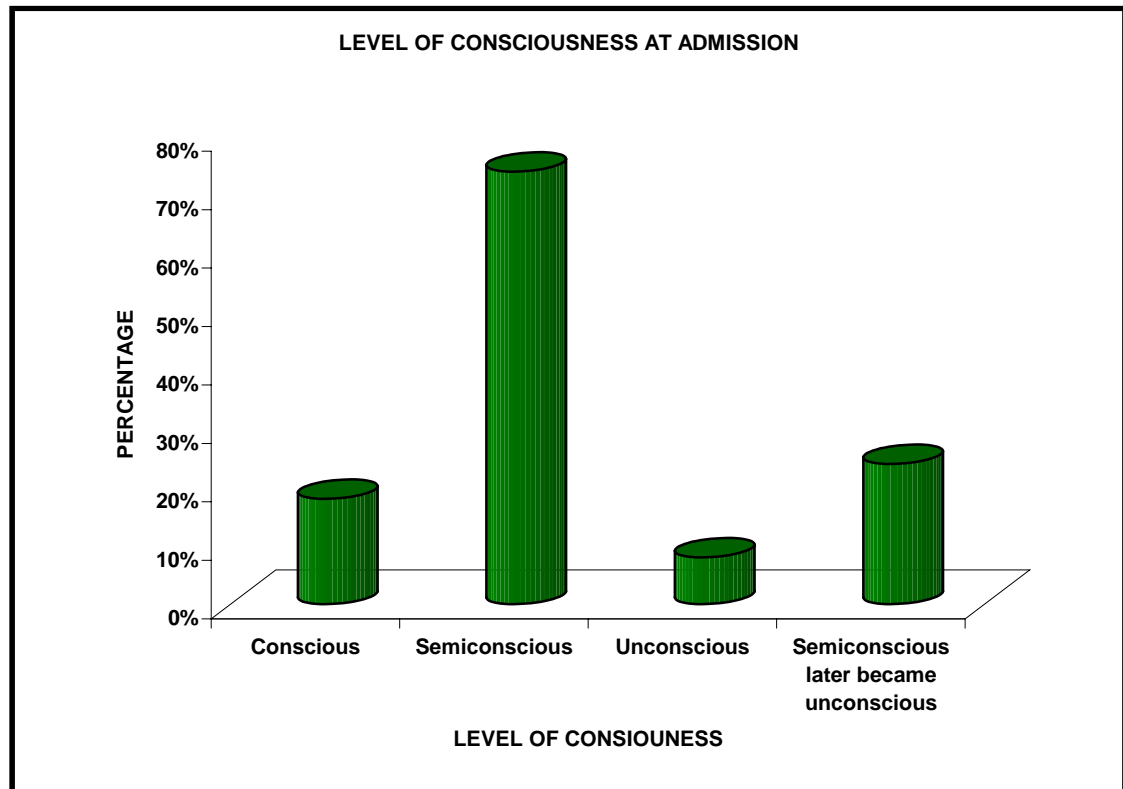
TABLE – VII

LEVEL OF CONSCIOUSNESS AT ADMISSION

Sl. No	Level of conscious	Number of patients	Percentage %
1.	Conscious	9	18%
2.	Semiconscious	37	74%
3.	Unconscious	4	8%
4.	Semiconscious later became unconscious	12	24%

The other one, of the 13-20 age group and a S-CRP level of <6 mg /L and a CSF picture in favour of viral infection, was treated with antibiotics and other supportive measures showed a good prognosis.

The remaining two cases between 21-40 years who were admitted in unconscious state, developed unconsciousness 48 hrs before admission which showed a delay in admission. One of them had a S-CRP level of <6 mg/L and CSF picture in favour of viral infection and not improved with adequate supportive measures, had only two days of hospitalization and expired. (Table – VII).



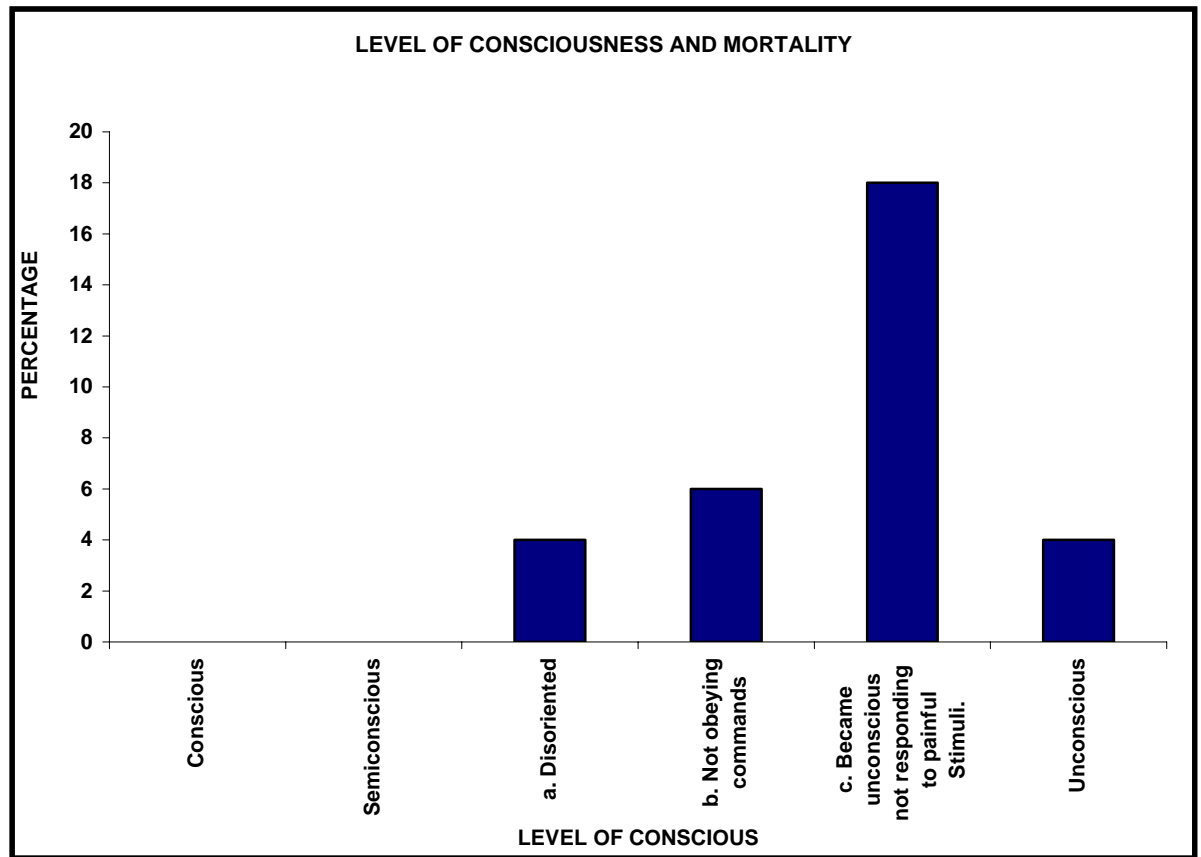
The other one was having Cheyne-Stoke breathing with papilledema and other clinical signs in favour of CNS infection. The C.T. scan was normal, but the serum C-reactive protein was found to be very high > 48 mg/L.

Thirty seven cases were found to be semiconscious on admission. The symptom duration before admission varied from few hours to three weeks. Twenty five cases were showing improvement with antibiotic treatment.

Twelve cases became unconscious soon after the admission and expired despite all possible supportive measures. Of the twelve cases, eight cases were of adolescent (13-20 years) age group, three cases were between 20-40 years and one between 40-60 years.

TABLE – VIII
LEVEL OF CONSCIOUSNESS AND MORTALITY

Sl. No	Level of conscious	Number of patients	Death	Percentage %
1.	Conscious	9	0	0
2.	Semiconscious			
	a. Disoriented	13	2	4
	b. Not obeying commands	13	3	6
	c. Became unconscious not responding to painful Stimuli.	11	9	18
3.	Unconscious	4	2	4



Among the three adults, one was a known case of pulmonary tuberculosis (by sputum examination). His CSF picture was in favour of a definite tuberculous meningitis positive for cobweb AFB stain and S-CRP levels of 24-48 mgs/L. He was not showing any improvement with adequate antibiotics, antituberculous drugs and steroid therapy. Patient developed hydrocephalus, confirmed by C.T. scan and expired. The other two adult cases were having a CSF picture in favour of viral infection and this is supported by low S-CRP levels of <6 mg/L. They did not improve with antibiotic treatment and expired. (Table – VIII).

Cerebrospinal Fluid

Lumbar puncture was done in all fifty cases. In seven cases, guarded lumbar puncture was done due to papilledema and bad clinical condition. In two cases the AFB staining was positive. (4%).

Ten cases had Gram positivity and seven had Gram negativity. All the seventeen were observed to have low CSF sugar value and with empirical treatment all the patients had good prognosis. Also all the 8 persons with S-CRP of 12-24 mg/l were Gram negative.

Seven cases were observed to have positive cob-web of which two were AFB positive. All the seven cases were found to have elevated proteins, normal or low sugar values in the CSF. The CSF culture was positive in twenty five of the fifty cases.

CSF Cell Count

There was significant pleocytosis in thirty six cases (of which seventeen cases were having elevation of polymorphonuclear cells which are usually absent in normal CSF, and nineteen cases had lymphocyte predominance. Ten cases were found to give positive results for Gram's staining as already stated. Eight cases were having S-CRP levels of more than 48 mg/L, 9 cases were having S-CRP level between 24 to 48 mg/L, 12 to 18 mg/L in 8 cases, 6mg/l in one case and <5mg/L in four cases. One of the four cases with CRP levels <5mg/l, three cases had a poor prognosis and expired. All the seventeen cases showed a marked fall in CSF sugar levels and elevated protein levels.

The other cases with S-CRP between – to ++, were having elevated CSF lymphocytes. In these groups, two cases were positive for AFB staining and seven for cob web suggestive of tuberculous meningitis. Five cases had levels of 24-48mg/L of which, one case had a bad prognosis, developed hydrocephalus and expired. In five cases the S-CRP levels were between 12 to 18 mg/L and 6 to 12mg/L in six cases of which one case expired who had elevated protein and normal sugar in CSF. Seven cases had S-CRP levels of <5mg/L of which three cases expired, all of them showed a near normal protein and sugar levels in CSF.

Positive Predictive Value Estimation

Twenty five cases had S-CRP of >12 mg/l. Of these, seventeen cases were diagnosed to have bacterial meningitis and eight cases of tuberculous meningitis.

$$PPV = TP / (TP + FP)$$

$$= 17 / (17 + 8)$$

$$= 17 / 25$$

$$= 68\%$$

PPV - Positive predictive value TP – True positive FP – False Positive

Sex and Mortality

The total mortality rate of the study was 28% (14 cases). Of which 18% (9 cases) were males and 10% (5 cases) were females. (Table – IX).

TABLE – IX

SEX AND MORTALITY

Sl. No	Prognosis	Sex	Number	Percentage %
1.	Survived	M	19	38%
		F	17	34%
2.	Dead	M	9	18%
		F	5	10%

Of the 72% cases who survived, 38% (19 cases) were males and 34% (17 cases) were females. It shows a male predominance in mortality rate also.

TABLE – X
AGE GROUP AND MORTALITY

Sl. No	Age in years	Number of Patients	Death	Percentage %
1.	13 – 20	16	8	16%
2.	21 – 40	14	2	4%
3.	41 – 60	16	2	4%
4.	> 60	4	2	4%

As shown in the Table – X, 8 cases of 13-20 years of age group expired, constituting a mortality rate of 16% and 4% each in all other age groups.



DISCUSSION

Meningeal infection still remains a significant health problem, although the overall incidence had decreased. The diagnosis and treatment of acute meningitis is a challenge for the primary care physician. The earlier the recognition of bacterial meningitis and the more rapid the institution of antimicrobial therapy, the better the chance of a favourable outcome. Since the modality of treatment for bacterial and viral meningitis are totally different, it is very important to differentiate the meningitis on aetiological basis from bacterial and viral origin.

It is generally held that the confirmation of viral meningitis by means of a positive culture is of academic interest, since no specific antiviral therapy exists to change the clinical outcome. The CSF examination is most critical in distinguishing bacterial from viral meningitis. When a definite diagnosis of viral meningitis is made, anti-microbial therapy could be discontinued and the hospital stay might be significantly shortened.

Not all medical centers have viral diagnostic laboratories at their disposal. Moreover, the serologic confirmation of a viral infection is usually of academic interest, since by the time its result is available, the patient has recovered and it never determines specific therapy. Therefore, several different techniques to discriminate rapidly between viral and bacterial meningitis have been evaluated. These include counter immunoelectrophoresis (CIE) of the cerebrospinal fluid

(CSF) for the detection of viral antigens and examination of the CSF for immunoglobulins, Lactic acid dehydrogenase, creatine phosphokinase isoenzyme and C-reactive protein (CRP).

The sine quo non of establishing viral meningitis on the basis of culture is very expensive and moreover it is not available in most of the places in our country and unfortunately no simple and easily performed procedure to distinguish viral from bacterial meningitis is available which has 100 percent predictive positive and negative values. For this reason the C reactive protein (CRP) was chosen to differentiate bacterial from viral infections of the central nervous system.

Abramson J.S. Hamton K.D. et al 1985¹ studied the use of C-reactive protein for differentiating meningitis and have pointed out that the C-reactive protein may be the single best non specific indicator of bacterial infection with sensitivity and specificity rates of 100 and 98 percent, respectively.

Further the serum C-reactive protein measured by rapid latex test can be done as a bedside procedure which cost only thirty rupees and two minutes time. If the result is viral, unnecessary antibiotics administration for prolonged period can be avoided, and only supportive measures are sufficient for all cases of viral meningitis. Even if the virus is isolated, at present no specific antiviral drug therapy is available.

Therefore, the serum C-reactive protein estimation is most useful in differentiating bacterial from viral infection of the central nervous system, especially for developing countries like ours, even in peripheral medical centers.

Sex Incidence

Meningeal infection both bacterial and viral has got a male predominance as observed in the study correlations well with the study of **National Institute of Communicable Diseases**⁶⁸, Directorate General of Health, India, during the epidemics of bacterial meningitis in the year 1966, 1985 and 1987. The male predominance of 69 percent was shown **Etter C.G. 1991**²⁶ in his study on viral meningitis.

Age Incidence

32% were in 13-20 years age group whereas 28% were in 21-40 years age group and 32% were in 41-60 age group, which correlates well with **Choi, C 1992**¹⁷ who has pointed out that meningitis remains a significant health problem for the older adults. Although the overall incidence of the disease has decreased, the incidence of meningitis in older adults is increasing and the recognition of meningitis in the older adults may be more difficult.

Symptoms

It is observed in the study that, fever is the most common presenting feature (98%) of meningeal infection compared to the 85% as per the study of **Rosa. K.L. et al (1991)⁸⁵** and **Feigin R.D. et al (1992)²⁸**. According to **Dufour J.F. (1991)²³** it is 80% whereas **Rasmussen, H., Nielsen, B. 1992⁸¹** stated an incidence of 79%.

Seizures were found in 42% of cases in the study whereas it is 30.4% in the study of **Pomeroy et al (1990)⁷⁶** and 30% by **Feigin R.D. et al in 1981²⁷**.

Signs

Altered sensorium was found in 82 percent of cases in the study as compared to 69% in the study of **Rasmussen H., Nielson. B., et al 1992⁸¹**. Further the altered sensorium was more commonly associated with viral meningoencephalities. **Tyler. K.L. in 1984¹⁰⁶** and **Whitely R.J in 1990¹¹³** noticed an increased incidence of altered sensorium in viral encephalitis when compared to bacterial meningitis.

Meningeal Signs

Neck stiffness was present in all cases as it was considered as the prime sign for the selection of cases. The Kernig's sign was present in 76% cases and the Brudzinski's sign in 60% of cases whereas **Feigin.R. D., et al in 1981²⁷** and **1992²⁸** have noticed only 50 percent of cases were having these meningeal signs. This was also supported by **Spanson et al in 1989⁹⁶** and **Rasmussen. H., Nielsen,**

B et al in 1992⁸¹. In another study, by **Dufour JF in 1991²³** the incidence of meningeal signs was over 80%.

Neurological Deficits

It is observed in the study that, hemiplegia with facial nerve involvement, was the commonest neurological deficit with an incidence of 12 percent isolated abducent nerve palsy unilateral or bilateral having an incidence of 10% tops the cranial nerve deficits whereas isolated facial nerve palsy and isolated aphasia were found in 8% of cases each and Quadripareisis in one case. The overall neurological deficits in the study was 40 percent, in contrast to the study of **Swartz MN et al 1965⁹⁸** and **Pomeroy LS et in 1990⁷⁶**, who have noticed an incidence of only 10% and 20% of neurological deficit in viral and bacterial meningitis respectively.

Serum C-Reactive Protein

The ability of serum C-reactive protein (S-SRP) to differentiate between acute bacterial and non-bacterial meningitis was evaluated in fifty cases, of adult population. The patients underwent lumbar puncture for suspected central nervous system (CNS) infections.

Of the fifty cases, 17 cases were diagnosed as bacterial meningitis, another 33 cases as meningitis due to non-bacterial causes. In patients with bacterial meningitis eight cases were having the S-CRP levels of more than 48 mg/L. The

S-CRP levels of 24-48 mg/l, were found in 9 cases. In eight cases, S-CRP was 12-24 mg/l. and were diagnosed as tubercular meningitis. There was no case of fungal or atypical meningitis in the study.

In nine cases the S-CRP levels were 6-12 mg/L. In sixteen cases the S-CRP was <5 mg/L. All the 25 cases were diagnosed as cases of viral meningitis.

Therefore, a significant positive S-CRP supported by.

1. Cerebrospinal fluid pleocytosis.
2. Elevated protein and low CSF sugar
3. A CSF sugar value of less than 35 mg/dl. was taken as evidence of bacterial aetiology.

From the study, in adults, a S-CRP level of less than 6 mg/l. with clinical signs of meningitis, is a definite indicator of viral meningitis. Whereas, a S-CRP level of more than 48 mg/l indicates a definite bacterial aetiology; this is supported by **Hensen. L., Kamin, W 1992⁴⁶ and Riberio, M.A. Kimura, R.T., 1992⁸³.**

As the patients who have shown a S-CRP level of 24-48 mg/l and 12-24 mg/L were having the history of preadmission treatment with antibiotics and steroids. These patients may have partially responded to the treatment, further the steroids might have reduced the S-CRP level. This view is supported by **Smith et al (1990)⁹⁴, and H. Gevold, H.E. et al in 1992³²** as per their studies, the steroids

inhibit macrophage secretion and synthesis of interleukin 1 the messenger and modulator for CRP stimulation from hepatocytes. In all these patients, the CSF analysis showed a definite possibility of bacterial meningitis. Therefore in patients, who give history of pre-admission treatment with steroids a S-CRP level of more than 48 mg/l may also indicate bacterial aetiology.

S-CRP and Prognosis

On serial monitoring, it is observed that a fall in the S-CRP concentration is a sensitive indicator of recovery from meningeal infections long before other signs.

Of the eight cases who had S-CRP level of more than 48 mg/L., 6 patients had a good prognosis which has been demonstrated by repeated S-CRP and by repeated lumbar puncture. 2 cases expired within 2 days of hospitalization despite adequate antibiotic therapy, they were unconscious at admission and had poor general condition.

To assess the prognostic value of S-CRP, the test was done first at admission, the second, 3 days after hospitalization and the third one before discharge. Six cases showed a rapid fall of more than 10 mg/L in S-CRP levels had a very good prognosis.

In one case the S-CRP levels showed a sustained high level. The repeated CSF examination showed near normal values in favour of a good prognosis. But

the patient developed hydrocephalus and expired despite all possible supportive measures. This shows that S-CRP is a better prognostic indicator than repeated CSF examination, thereby reducing the repeated invasive techniques. This is consistent with the study of **Kobli V, and Singh. S. (1993)**⁵⁷.

Macfarlane⁶² reported 97% sensitivity and 98% specificity to differentiate bacterial from viral meningitis by means of CRP testing. Whereas **Benjamin**¹¹ observed the test to be less sensitive i.e. 66% while **Gutterberg**⁴⁰ found it to be useless, **Gupta D. 1987**³⁹ observed a sensitivity of 60% and specificity of 92% in distinguishing bacterial and viral meningitis. The S-CRP level of more than 48 mg./L was taken as the cut off point for pyogenic meningitis. In distinguishing partially treated pyogenic meningitis from tuberculous meningitis, CRP had a positive predictive value of 90%.

Mortality

It is observed from the study that, the overall case fatality rate was 28% (14 cases). All these cases were found to have altered sensorium at the time of admission. This indicates an increase in case fatality rate in patients who had an altered level of consciousness at the time of admission and is supported by the study of **Deivanayagam N et. al, clinical epidemiology unit, Madras Medical College in 1993**²¹, who pointed out a case fatality rate of 22% particularly in cases who had an altered level of consciousness on admission.

In the study, the survival rate was 72% where as the study of **Rasmussen H, Nielsen B., et al in 1992⁸⁰** stated a survival rate of only 63% and fatality rate of 37% probably due to late arrival to hospital.

The mortality rate also shows a male predominance of 18 percent whereas the incidence in females is 10 percent. Bacterial meningitis consists of 6% mortality whereas viral meningitis has a mortality rate of 22%.

Others

It is observed in the study that the cerebrospinal fluid culture was positive in 50% and the Gram's stain was informative in 34% of cases whereas, AFB staining was informative in only 4% cases. This is in contrast to 65% positivity of culture and 54% in Gram's stain as reported by **Bohr. V. et al in 1983¹²**.

Further, the culture positivity fall from 65% to 38% and the Gram's stain positivity from 54% to 34% among patients with prior antibiotic use, supported by **Bohr. V. et al¹², Rasmussen N, Hensen, B et al 1983⁸¹**.

As the antibiotics are freely used in all patients with fever irrespective of the age group, a positive culture or cerebrospinal fluid biochemistry may be difficult to achieve as per the study of **Jiao F.Y., Ceo. H.C., et al 1992⁵³**.

CONCLUSION

1. Estimation of C-reactive protein in serum is the cheapest, sensitive and specific test to differentiate bacterial from viral infections.
2. It is a simple qualitative as well as quantitative test and can be done as a bed side investigation.
3. With serum C-reactive protein, a definite aetiological diagnosis can be made rapidly at the time of admission itself.
4. A serum CRP level of less than 6 mg/l with clinical signs of meningeal infection is a definite indicator of viral meningitis.
5. A serum CRP level of more than 48 mg/l with clinical signs of meningeal infection is a definite indication of bacterial meningitis.
6. Preadmission treatment with steroids cause a fall in CRP levels in bacterial meningitis.
7. Serum CRP has 68% predictive value in adults.
8. The rapid differentiation facilitates an early, accurate and appropriate therapy thereby reducing the mortality and morbidity rates, the overall cost of the treatment and the duration of hospitalization.

9. Serum CRP can be used as the best and most sensitive bedside prognostic indicator of bacterial infections.
10. Meningeal infections have a definite male predominance.
11. Altered level of consciousness at the time of admission is associated with bad prognosis and high case fatality rate (28%)
12. Fever is the commonest presenting feature followed by altered sensorium, symptoms of increased intracranial tension and seizure. Among neurological deficits, hemiparesis, VIth cranial nerve palsy and VIIth cranial nerve palsy were found to be common.
13. The earlier the recognition of bacterial meningitis and more rapid the institution of antimicrobial therapy the better the chance of a favourable outcome.
14. Therefore, the serum C-reactive protein estimation is most useful in differentiating bacterial meningitis from viral meningitis, especially for developing countries like India, even in peripheral health centres.

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PROFORMA

1. Sl. No. :
2. Name :
3. Age :
4. Sex :

5. QUESTIONNAIRE OF THE SYMPTOMS:

- | | | | |
|------|---------------------------------------|--------|--------|
| i) | Whether the patient had Fever? | 1. Yes | 2. No. |
| ii) | Whether the patient had vomiting? | 1. Yes | 2. No. |
| iii) | Whether the patient had headache? | 1. Yes | 2. No. |
| iv) | Whether the patient had Seizures? | 1. Yes | 2. No. |
| v) | Whether the patient has any weakness? | 1. Yes | 2. No. |

6. CLINICAL EXAMINATION:

A - PULSE

B - BLOOD PRESSURE

C - RESPIRATORY RATE

D - TEMPERATURE

E - GENERAL EXAMINATION

F - SYSTEMIC EXAMINATION

I. CENTRAL NERVOUS SYSTEM

1. Neck Rigidity
2. Kernig's sign
3. Brudzinski's sign
4. Cranial Nerve involvement
5. Papilledema

II. CARDIOVASCULAR SYSTEM

III. RESPIRATORY SYSTEM

IV. ABDOMEN

7. INVESTIGATIONS:

BLOOD:

- Haemoglobin
- Total Count
- Differential Count
- Erythrocyte sedimentation rate

8. X-RAY CHEST PA - VIEW

9. SPECIAL INVESTIGATIONS:

A – SERUM C – REACTIVE PROTEIN (S-CRP)

B -CEREBRO SPINAL FLUID

- Cell Count
- Glucose
- Protein
- Culture
- AFB
- Gram's stain

10. PROGNOSI

Sl. No.	Name	Age	Sex	Neck Rigidity	Fever	Kerning	Brudzinski	Cranial N	CVA	Altered Sensorium	Headache	Vomiting	Seizures	Papilledema	S-CRP	CSF Cell	CSF-glucose	CSF-Protein	Prognosis	Culture	AFB	Gram's Stain
1	HUSSAIN BASHA	20	M	+	+	+	+	-	-	+	+	+	+	-	-	L	39	46	D	-	-	-
2	JOSEPH	18	M	+	+	+	-	+	-	+	+	+	+	+	3+	PMN	26	55	D	+	-	+
3	KUMAR	19	M	+	-	+	+	-	-	+	-	-	-	-	-	L	40	44	D	-	-	-
4	JAYARAMAN	18	M	+	+	+	-	-	+	+	+	-	+	+	3+	PMN	23	60	D	+	-	+
5	VIMAL	16	M	+	+	+	+	+	-	+	-	-	+	-	2+	L	28	50	A	+	+	-
6	VIGNESH	15	M	+	+	-	-	-	-	+	-	-	-	-	4+	L	29	62	A	+	-	-
7	KUPPUSAMY	20	M	+	+	+	+	+	-	+	-	-	+	-	2+	L	30	49	D	-	-	-
8	SRINATH	14	M	+	+	+	+	-	-	-	-	-	-	-	4+	PMN	22	61	A	+	-	+
9	KRISHNAVENI	19	F	+	+	+	+	+	-	+	+	+	+	+	3+	PMN	23	59	D	+	-	-
10	KALPANA	18	F	+	+	+	+	-	-	+	+	+	-	-	1+	L	27	52	A	-	-	-
11	SHYAMALA	15	F	+	+	+	-	-	-	+	+	+	-	-	2+	L	28	56	A	+	-	-
12	GAYATHRI	17	F	+	+	-	-	-	-	+	+	-	-	-	3+	PMN	19	60	A	+	-	+
13	KAVITHA	18	F	+	+	+	+	-	+	+	-	-	-	-	-	L	40	43	D	-	-	-
14	ANITHA	17	F	+	+	+	+	-	-	+	+	+	-	-	3+	PMN	21	51	A	+	-	+
15	FATHIMA	17	F	+	+	+	+	-	-	+	+	-	-	-	2+	L	30	48	A	+	-	-
16	FARITHA BEGAM	18	F	+	+	+	+	-	-	+	-	-	-	-	-	L	39	42	D	-	-	-
17	RAVI	35	M	+	+	+	+	-	-	+	-	-	-	-	+	L	38	44	A	-	-	-
18	BASKAR	23	M	+	+	-	-	-	-	+	-	-	-	-	4+	PMN	18	63	A	+	-	+
19	CHAKARABANI	36	M	+	+	+	+	-	-	+	+	+	+	-	-	L	37	43	D	-	-	-
20	KANNAIYAN	34	M	+	+	-	-	-	-	+	-	-	-	-	-	L	37	40	A	-	-	-
21	MUTHU	28	M	+	+	+	+	-	-	+	+	+	-	-	2+	L	26	49	A	+	-	-
22	BALA	22	M	+	+	+	+	+	-	+	+	+	+	-	4+	PMN	18	62	A	+	-	+
23	VAIRAVEL	36	M	+	+	+	+	-	-	-	+	+	-	-	1+	L	33	47	A	-	-	-
24	VELAYUTHAM	25	M	+	+	+	+	-	+	+	+	+	+	-	-	L	38	43	D	-	-	-
25	VINOTHINI	24	F	+	+	+	+	-	-	+	+	-	-	-	2+	L	28	49	A	+	+	-

Sl. No.	Name	Age	Sex	Neck Rigidity	Fever	Kerning	Brudzinski	Cranial N	CVA	Altered Sensorium	Headache	Vomiting	Seizures	Papilledema	S-CRP	CSF Cell	CSF-glucose	CSF-Protein	Prognosis	Culture	AFB	Gram's Stain
26	INDRA	39	F	+	+	+	+	-	-	+	+	-	-	-	1+	L	30	49	A	-	-	-
27	BHUVANESWARI	33	F	+	+	-	-	-	-	+	-	-	+	-	3+	PMN	24	58	A	+	-	+
28	KAMALA	39	F	+	+	+	+	+	-	+	+	+	+	-	-	L	36	44	A	-	-	-
29	RANGITHAM	37	F	+	+	+	+	+	-	+	-	-	-	-	-	L	38	44	A	-	-	-
30	SHENBAGA VALLI	37	F	+	+	+	-	-	-	-	-	-	-	+	4+	PMN	21	60	A	+	-	-
31	SELVAM	45	M	+	+	+	+	-	-	+	-	+	+	+	4+	PMN	23	54	A	+	-	+
32	RADHAKRISHNAN	53	M	+	+	+	+	-	-	+	+	-	-	-	2+	L	31	49	A	+	-	-
33	KUTTIAPPAN	55	M	+	+	+	+	-	+	-	+	+	+	-	-	L	38	45	D	-	-	-
34	SENTHILMURUGAN	43	M	+	+	-	-	-	-	+	+	+	+	-	1+	L	30	51	A	-	-	-
35	ARASAPPAN	49	M	+	+	+	+	-	-	+	-	-	-	-	1+	L	32	50	A	-	-	-
36	VISWANATHAN	45	M	+	+	+	+	-	-	+	+	+	+	+	4+	PMN	18	56	A	+	-	+
37	DURAISELVAN	41	M	+	+	+	+	-	-	+	+	+	+	-	-	L	35	40	A	-	-	-
38	KANNAPPAN	57	M	+	+	-	-	-	-	-	-	+	-	-	4+	PMN	20	58	A	+	-	-
39	MANNANGATTI	52	M	+	+	-	-	-	-	-	+	+	-	-	-	L	35	42	A	-	-	-
40	SAMYKANNU	48	M	+	+	+	+	+	-	+	+	+	+	-	1+	L	30	50	A	-	-	-
41	SENBAGAVALLI	47	F	+	+	-	-	-	-	+	-	-	-	-	1+	L	28	55	A	-	-	-
42	BEEBI JOHN	53	F	+	+	+	-	+	+	+	+	+	-	-	1+	L	28	58	A	-	-	-
43	MARIYAMMAL	56	F	+	+	+	+	-	+	-	-	-	-	-	-	L	38	45	A	-	-	-
44	AMSAVALLI	44	F	+	+	-	-	-	-	+	+	+	-	-	2+	L	29	50	A	+	-	-
45	JAYALAKSHMI	54	F	+	+	+	+	-	-	-	-	-	+	-	-	L	36	40	D	-	-	-
46	LAKSHMI	41	F	+	+	+	+	-	-	+	+	+	-	-	3+	PMN	20	58	A	+	-	-
47	NADESAN	66	M	+	+	+	-	-	-	+	+	-	-	-	-	L	36	41	A	-	-	-
48	RAMASAMY	63	M	+	+	-	-	-	-	+	+	+	+	+	3+	PMN	18	62	A	+	-	-
49	JOTHI	63	F	+	+	+	-	-	-	-	-	-	-	-	3+	PMN	22	59	D	+	-	-
50	ARIYAMMAL	75	F	+	+	+	-	+	-	+	+	+	+	-	-	L	39	43	D	-	-	-